II. REMARKS

Introductory Comments

Claims 21-27 were examined in the Office Action under reply. Claims 23 and 24 were indicated as allowable if rewritten in independent form and claims 21, 22 and 25-27 were rejected under 35 U.S.C. § 112, first paragraph. These grounds of rejection are believed to be overcome by this response and are otherwise traversed for reasons discussed in detail below.

Overview of the Above Amendments

Claim 22 has been cancelled and the recitations from claim 22 have been incorporated into claim 21. Claim 21 has also been amended to recite that delivery is via a pump. Finally, claim 21 has been amended to delete the term "pharmaceutical," as suggested by the Examiner in a telephone conversation with the undersigned on May 5, 2004.

Claims 23 and 24 have been amended to depend from claim 21. Claims 26 and 27 have been amended to recite that distribution is "over an area of at least about 50 mm^2," and to depend from claims 21 and 23, respectively. The Examiner suggested applicants amend claims 26 and 27 to read "at least 50 mm^2" in the telephone discussion of May 5, 2004. New claim 28 is identical to claims 26 and 27 as amended, except that it depends from claim 24.

New claims 29-34 have been added. New independent claim 29 is similar to claim 21 as amended with the exception that it omits "wherein said recombinant adeno-associated virus virions are administered by convection enhanced delivery using a pump" and instead recites that administering is "at a rate of 0.4 µl per minute or less." New claim 30 depends from claim 29 and recites that "virions are administrated using convection enhanced delivery (CED) using a means for CED pumping." New claims 31 and 32 depend from claim 29 and recite CED using an infusion pump and an osmotic pump, respectively. New claims 33 and 34 depend from claim 29 and recite that administering is "at a rate of 0.2 µl per minute or less" and "at a rate of 0.1 µl per minute or less," respectively.

The foregoing amendments are made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record.

Applicant expressly reserves the right to file one or more continuing applications containing the unamended claims.

Rejections Under 35 U.S.C. § 112, First Paragraph:

Claims 26 and 27 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner acknowledges Figures 1B and 3B show "about 49 mm^2 for IP and about 45 mm^2 for OP in Figure 3B, and about 50 mm^2 in Figure 1B." Office Action, pages 1-2, bridging paragraph. However, the Examiner alleges the phrase "over an area of at least 40-50 mm^2," is new matter. Applicants respectfully disagree. In fact, as shown in Figures 1B and 3B, the range of delivery varies and can include delivery over areas as great as 40-50 mm^2 or more. Nevertheless, solely in an effort to advance prosecution, claims 26 and 27 have been amended to recite that the recombinant AAV virions are distributed over an area of at least about 50 mm^2, acknowledged by the Examiner to be supported by the disclosure. Thus, this basis for rejection has been overcome and withdrawal thereof is respectfully requested.

Claims 21, 22 and 25 remain rejected under 35 U.S.C. § 112, first paragraph, as non-enabled. The Office argues:

> The specification fails to provide adequate guidance and evidence for how to deliver a rAAV virus expressing a protein to the brain of a subject via any administration route or administration apparatus to the brain other than infusion pump and osmotic pump such that the rAAV virus is distributed in the brain over an area greater than 5 mm^2.
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> [I]t is apparent that is was unpredictable at the time of the invention whether the administered rAAV vector would be distributed to an area greater than 5 mm^2 in the brain of a subject via various administration routes or apparatuses that is either manual injection or mechanic method or pump other than osmotic pump and infusion pump, or electroporation, etc. Thus, one skilled in the art at the time of the invention would not know how to use the invention commensurate in scope with these claims.

Office Action, pages 4-5. Applicants respectfully submit the claims are indeed enabled throughout their scope. However, solely in order to advance prosecution, applicants have cancelled claim 22 and amended claim 21 to recite that "said recombinant adeno-associated virus

virions are administered by convection enhanced delivery using a pump." Claim 21 as amended finds support in original cancelled claim 22 with respect to CED, and at p. 27 and Example 2 (pp. 34-35) where both infusion pumps and osmotic pumps are disclosed as pumps for delivery of vector by CED.

Applicants' charge under 35 U.S.C. §112, first paragraph is to provide a specification that teaches one of ordinary skill in the art *how to make and use* the claimed invention without "undue experimentation." *In re Wright*, 27 USPQ2d 1510 (Fed. Cir. 1993). Nothing more than objective enablement is required, and such enablement is judged by the standards of those skilled in the art. A specification which teaches *how to make and use* the invention in terms which correspond in scope to the claims must be taken as complying with the first paragraph of §112 unless there is reason to doubt the objective truth of the statements relied upon therein for enabling support. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). Thus, when the PTO makes a rejection for failure to teach how to make and/or use the invention, the PTO must explain its reasons for the rejection and support the rejection with (i) acceptable evidence, or (ii) reasoning which contradicts applicants' claim. The reasoning must be supported by current literature as a whole and the PTO must prove the disclosure requires undue experimentation. *In re Marzocchi*, 169 USPQ 367, 369-70 (CCPA 1971). For the reasons detailed below, and in light of the present amendments to the claims, the Office has failed to establish a *prima facie* case of nonenablement.

In particular, the examples in the present application clearly set forth procedures for using two widely divergent pumps, an osmotic pump and an infusion pump. These pumps differ in several aspects, not the least of which is that osmotic pumps are self-powered and function by simple osmosis, while infusion pumps generally require an energy source. Applicants have provided working examples of their invention using two completely different pumps. This, in and of itself, is enough to satisfy the enablement requirement for a generic claim directed to the use of a pump in order to achieve the claimed distribution.

Moreover, it is axiomatic that a patent specification "need not teach, and preferably omits, what is well known in the art." See, *Spectra-Physics, Inc. v. Coherent, Inc.* 3 USPQ2d 1737, 1743 (Fed. Cir. 1987); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986). In the present case, one need only do a search of the PTO patents database to

find innumerable patents detailing various pumps and methods of using these pumps. One of skill in the art could readily adapt many of these pumps for use with the present invention using the guidance present in the application. Additionally, one of skill in the art could easily test for distribution of rAAV virions using methods well known in the art and detailed in the application. The Office is reminded that even a large amount of experimentation is permitted under §112, first paragraph, provided it is routine. *Ex parte Jackson*, 217 USPQ 804, 807 (POBA 1982) (a claim is acceptable under §112 even if it requires extensive experimentation, as long as the experimentation is routine).

Contrary to the Office's assertions, and in light of the present amendments to the claims, applicants have indeed adequately taught how to make and use the claimed invention such that one of skill in the art could readily practice the invention without an undue amount of experimentation. In light of the disclosure in the application, and in view of the state of the art, applicants submit that the present claims are indeed enabled. Reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §112, first paragraph, is respectfully requested.

New Claims:

New claims 29–34 have been added. These claims relate to methods wherein the composition comprising recombinant adeno-associated virus virions is delivered at or below a specified rate, such as 0.4, 0.2 and 0.1 µl per minute. *See* claims 29, 33 and 34. Delivery by CED at these infusion rates is adequately supported in the specification at Table 2 (p. 48), which discloses infusion rates of 0.4, 0.2 and 0.1 µl per minute, and also in Example 2 (pp. 34, 39), which discloses a delivery rate of 8 µl per hour (0.133 µl per minute) for both infusion and osmotic pumps.

New claim 30 recites that CED is accomplished using a means for CED pumping. Claim 30 finds support in original claim 1 (and cancelled claim 22) with respect to CED, and at p. 27 and Example 2 (pp. 34-35) where both infusion pumps and osmotic pumps are disclosed as means for delivering vector by CED. New claims 31 and 32, reciting CED using and infusion pump and an osmotic pump, respectively, are supported by original claims 2 and 3, and are similar to pending claims 23 and 24.

III. CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and request early notification to that effect. If the Examiner notes any further matters which he believes may be resolved by a telephone interview, he is encouraged to contact Christina Thomson by telephone at (510)748-7208, or by fax at (510)748-7368.

Respectfully submitted,

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